DEAR EDITOR:

I enjoyed Dr. Feifel's article, "When common clinical practice meets evidence-based medicine," in the December issue of *Psychiatry 2006*. My common practice is to increase the dose of an antidepressant until the person has a positive response. After several months at this dose, I will attempt to decrease the medication to the lowest possible dose. Do you have any thought as to why this will work in some patients and not others? I am often decreasing the dose and having horrible depression symptoms return. I will increase the dose and the symptoms remit. As there are so many different patients with so many different responses to medications, has anyone studied populations who do not respond to a low dose of an SSRI but do respond to higher doses? Is there the thought that it takes more time or more medication to achieve the response? Are these patients' reuptake transporters 100-percent blocked at the lower dose? Or does it take a higher does to achieve this? Is there a difference in the percentage blocked at two weeks versus eight weeks?

As a private practioner, I am in the people practice, and sending a patient out with a wish and a prayer ("Just hang in there on this dose for a couple more weeks.") is something I cannot do. An increase in dose not only gives them more medication it gives them the most important ingredient in fighting the depression battle—hope.

With regards,
Colleen A. Blanchfield, MD
Neuropsychiatrist
Reston, Virginia

AUTHOR RESPONSE

Dr. Blanchfield raises an interesting phenomenon. When I describe the existing medical evidence that fails to support increasing SSRI dose beyond the minimal therapeutic dose, I often hear the retort, "What about my patients on high-dose SSRIs who consistently relapse when I try to lower the dose." Of course research only addresses "average" effects of groups and cannot rule out that for any given individual a dose increase of his or her SSRI is responsible for producing a superior clinical response. However, we should be careful not to view the fact that a patient on high-dose SSRI relapses when the dose is lowered as validation that he or she requires the high dose to treat his or her depression in the first place. Antidepressant withdrawal relapse may be a completely separate phenomenon from the initial treatment effect. Important in this regard are studies conducted using specially concocted drinks that can rapidly reduce serotonin or noradrenaline/dopamine in the central nervous system of human subjects.[1] Those studies have shown that neither depletion of serotonin nor noradrenaline/dopamine induce depression in nondepressed, unmedicated patients. However, depressed patients who have been stabilized on SSRI medications and continue to take it will experience rapid relapse of their depression when given a drink that depletes their serotonin but will not experience rapid depression from drinks that deplete their noradrenaline/dopamine. Conversely, patients who are on maintenance treatment with serotonin-norepinephrine reuptake inhibitor medication will relapse when given a drink that depletes noradrenaline/dopamine but not when given a drink depleting serotonin. From these studies, it seems that that treating a patient with an antidepressant induces physiological changes that make that patient "mood-dependent" on the neurotransmitter system that is stimulated by the antidepressant such that rapid depletion of that neurotransmitter induces a "rebound" worsening of mood. Patients who are on high-dose antidepressants may be experiencing a related phenomenon when their dose is lowered.

REFERENCE

1. Delgado PL. Monoamine depletion studies: Implications for antidepressant discontinuation syndrome. *J Clin Psychiatry* 2006;67 Suppl 4:22–6. Review.

With regards,
David Feifel, MD, PhD
Department of Psychiatry, University of California, San Diego Medical Center, San Diego, California